

Reviewer: Rick J. Whiting
Risk Manager (EPA): 23

Date: February 15, 2011

STUDY TYPE: Primary Eye Irritation - Rabbit; OCSPP 870.2400; OECD 405

TEST MATERIAL: GF-2633 (Triisopropanolamine salt of Aminopyralid – 8.28 wt%; 2,4-D, dimethylamine salt – 42.2 wt%; Lot No. F1506-50, TSN032903-0001; pH: 7-8; soluble in water; clear liquid)

CITATION: Durando, J. (2010) GF-2633: Primary Eye irritation Study in Rabbits. Project Number: 101016, 29949. Unpublished study prepared by Eurofins/Product Safety Laboratories. 34 p. August 2, 2010. MRID 48173006

SPONSOR: The Dow Chemical Company, Midland, MI 48674

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 48173006), 0.1 mL of GF-2633 (Triisopropanolamine salt of Aminopyralid – 8.28 wt%; 2,4-D, dimethylamine salt – 42.2 wt%; Lot No. F1506-50, TSN032903-0001; pH: 7-8; soluble in water; clear liquid) was instilled as received into the conjunctival sac of the right eye of three young adult female New Zealand White rabbits (age: 12 weeks; weight: 2157-2224 g; source: Robinson Services, Inc., Clemmons, NC). The other untreated eye served as a control. Proparacaine was instilled immediately after dosing the second animal and prior to dosing for the third animal only. There was no need to further use of anesthetic during the study. Ocular irritation was evaluated using a high-intensity white light in accordance with Draize et al (1944) at 1, 24, 48 and 72 hours and at 4, 7, 10, 14, 17 and 21 days post-instillation.

Corneal opacity (score of 1) was observed in 3/3 rabbits from 1 hour through Day 14, in 2/3 rabbits on Day 17 and in 1/3 rabbits on Day 21. Iritis (score of 1) was observed in 3/3 rabbits from 1 hour through Day 21. Conjunctival redness (score of 2) was observed in 3/3 rabbits from 1 hour through Day 10 and in 2/3 rabbits on Day 14 and 17. Conjunctival redness (score of 1) was observed in 1/3 rabbits on Day 14 and 17 and in 3/3 rabbits on Day 21. Conjunctival chemosis (score of 2) was observed in 3/3 rabbits from 1 hour through Day 7 and in 1/3 rabbits on Day 17 and 21. Conjunctival chemosis (score of 1) was observed in 3/3 rabbits on Day 10 and 14, in 2/3 rabbits on Day 17 and 1/3 rabbits on Day 21. Conjunctival discharge (score of 2) was observed in 3/3 rabbits from 1 hour through Day 4, in 1/3 rabbits on Days 7, 10, 14, 21 and in 2/3 rabbits on Day 17. Conjunctival discharge (score of 1) was observed in 2/3 rabbits on Days 7, 10 and 14 and in 1/3 rabbits on Day 17 and 21. A white discharge was evident for two treated eyes between 72 hours and Day 4 and for one treated eye between 24 hours and Day 7. The maximum average irritation score of 37.0 was recorded 1 hour after test material instillation.

In this study, the formulation was considered corrosive. GF-2633 is classified as EPA Toxicity Category I for primary eye irritation.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OCSPP 870.2400; OECD 405) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

A. Observations: Corneal opacity (score of 1) was observed in 3/3 rabbits from 1 hour through Day 14, in 2/3 rabbits on Day 17 and in 1/3 rabbits on Day 21. Iritis (score of 1) was observed in 3/3 rabbits from 1 hour through Day 21. Conjunctival redness (score of 2) was observed in 3/3 rabbits from 1 hour through Day 10 and in 2/3 rabbits on Day 14 and 17. Conjunctival redness (score of 1) was observed in 1/3 rabbits on Day 14 and 17 and in 3/3 rabbits on Day 21. Conjunctival chemosis (score of 2) was observed in 3/3 rabbits from 1 hour through Day 7 and in 1/3 rabbits on Day 17 and 21. Conjunctival chemosis (score of 1) was observed in 3/3 rabbits on Day 10 and 14, in 2/3 rabbits on Day 17 and 1/3 rabbits on Day 21. Conjunctival discharge (score of 2) was observed in 3/3 rabbits from 1 hour through Day 4, in 1/3 rabbits on Days 7, 10, 14, 21 and in 2/3 rabbits on Day 17. Conjunctival discharge (score of 1) was observed in 2/3 rabbits on Days 7, 10 and 14 and in 1/3 rabbits on Day 17 and 21. A white discharge was evident for two treated eyes between 72 hours and Day 4 and for one treated eye between 24 hours and Day 7.

Individual Scores for Ocular Irritation

READING	RABBIT NUMBER	CORNEAL OPACITY	IRITIS	CONJUNCTIVA*		
				Redness	Chemosis	Discharge
1 Hour	3401	1	1	2	2	2
	3402	1	1	2	2	2
	3403	1	1	2	2	2
24 Hours	3401	1	1	2	2	2
	3402	1	1	2	2	2
	3403	1	1	2	2	2
48 Hours	3401	1	1	2	2	2
	3402	1	1	2	2	2
	3403	1	1	2	2	2
72 Hours	3401	1	1	2	2	2
	3402	1	1	2	2	2
	3403	1	1	2	2	2
Day 4	3401	1	1	2	2	2
	3402	1	1	2	2	2
	3403	1	1	2	2	2
Day 7	3401	1	1	2	2	1
	3402	1	1	2	2	1
	3403	1	1	2	2	2
Day 10	3401	1	1	2	1	1
	3402	1	1	2	1	1
	3403	1	1	2	1	2
Day 14	3401	1	1	2	1	1
	3402	1	1	1	1	1
	3403	1	1	2	1	2

*Score of 2 or more required to be considered "positive."

READING	RABBIT NUMBER	CORNEAL OPACITY	IRITIS	CONJUNCTIVA*		
				Redness	Chemosis	Discharge
Day 17	3401	1	1	2	1	1
	3402	0	1	1	1	2
	3403	1	1	2	2	2
Day 21	3401	0	1	1	0	0
	3402	0	1	1	1	1
	3403	1	1	1	2	2

*Score of 2 or more required to be considered “positive.”

The incidence of positive effects, severity and reversibility are detailed below:

Time Post Instillation	Incidence of Positive Effects		
	Corneal Opacity	Iritis	Conjunctivitis
1 Hour	3/3	3/3	3/3
24 Hours	3/3	3/3	3/3
48 Hours	3/3	3/3	3/3
72 Hours	3/3	3/3	3/3
Day 4	3/3	3/3	3/3
Day 7	3/3	3/3	3/3
Day 10	3/3	3/3	3/3
Day 14	3/3	3/3	3/3
Day 17	2/3	3/3	3/3
Day 21	1/3	3/3	3/3

Time Post Instillation	Severity of Irritation – Mean Score
1 Hour	37.0
24 Hours	35.3
48 Hours	35.3
72 Hours	33.7
Day 4	32.0
Day 7	27.3
Day 10	25.3
Day 14	21.3
Day 17	17.7
Day 21	12.7

B. Results: In this study GF-2633 was considered corrosive. The maximum average irritation score of 37.0 was recorded 1 hour after test material instillation.

C. Reviewer’s Conclusions: TRB agrees with the study author’s conclusions. GF-2633 is classified as EPA Toxicity Category I.

D. Deficiencies: None.